Evidence for a frontal cortex role in mediating both auditory and somatosensory habituation: A MEG study.

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Abstract

Magnetoencephalography (MEG) was used to investigate auditory and somatosensory responses to paired stimuli for commonality of frontal activation that may be associated with gating. A paired stimulus paradigm for each sensory evoked study tested right and left hemispheres independently in ten normal controls. MR-FOCUSS, a current density technique, imaged simultaneously active cortical sources. Each subject showed source localization, in the primary auditory or somatosensory cortex, for the respective stimuli following both the first (S1) and second (S2) impulses. Gating ratios for the auditory M50 response, equivalent to the P50 in EEG, were 0.54 ± 0.24 and 0.63 ± 0.52 for the right and left hemispheres. Somatosensory gating ratios were evaluated for early and late latencies as the pulse duration elicits extended response. Early gating ratios for right and left hemispheres were 0.69 ± 0.21 and 0.69 ± 0.41 while late ratios were 0.81 ± 0.41 and 0.80 ± 0.48. Regions of activation in the frontal cortex, beyond the primary auditory or somatosensory cortex, were mapped within 25 ms of peak S1 latencies in 9/10 subjects during auditory stimulus and in 10/10 subjects for somatosensory stimulus. Similar frontal activations were mapped within 25 ms of peak S2 latencies for 75% of auditory responses and for 100% of somatosensory responses. Comparison between modalities showed similar frontal region activations for 17/20 S1 responses and for 13/20 S2 responses. MEG offers a technique for evaluating cross modality gating. The results suggest similar frontal sources are simultaneously active during auditory and somatosensory habituation.

Introduction

Habituation to redundant sensory input, or sensory gating, has been studied utilizing electroencephalography (EEG) recordings of a paired click auditory stimulus. These studies have largely focused on habituation of the primary auditory response approximately 50 ms after presentation of the stimulus (P50). Gating is the reduction in amplitude of response to the second click relative to the first click measured as the event-related brain potential (ERP). The mechanisms responsible for habituation are hypothesized to protect higher cortical centers from flooding with irrelevant information (Venables 1964; Boutros 1991, 2004; Freedman 1998) and to protect processing of the first response by filtering redundant sensory inputs (Edgar 2005; Thoma 2007). These studies are of importance for consistently showing gating deficit in schizophrenia populations.

Localization of the P50 generators has not yielded consensus largely due to limitations with the spatial resolution of scalp-recorded EEG/ERP reconstructions (Barkley 2004). Magnetoencephalography (MEG) can overcome the conductivity and resistivity variations with both high spatial and temporal resolution (Hamalainen 1993; Hari 1998; Tepley, 2005). MEG has been used to evaluate auditory gating with the magnetic equivalent of the P50, designated the M50 response (Huotilainen 1998). Many MEG auditory studies have modeled brain response as equivalent current dipoles (ECDs) with gating ratios similar to EEG results for normal subjects (Clementz 1997; Weisser 2001; Huang 2003; Thoma 2003; Hanlon 2005). Garcia-Rill, et al used current density reconstruction of MEG recordings to localize the M50 response to multiple sources, usually including the frontal lobe, suggesting diffuse arousal-related projections in the cortex (Garcia-Rill 2008).

Somatosensory gating has been examined using a mixed modality paradigm consisting of paired auditory clicks and paired median nerve stimulation using EEG (Arnfred 2001; Kisley 2006) and MEG (Kakigi 2000, Thoma 2005, 2007), though no specific correlation between the auditory and somatosensory gating ratios has been determined. Our preliminary work has shown somatosensory gating of early latency response in the primary somatosensory cortex to paired finger taps accompanied by simultaneous frontal activation (Bowyer 2006). We performed an auditory evoked study of normal subjects complimented with a somatosensory evoked study. This study aimed to utilize current density MEG reconstruction to define magnetic auditory and somatosensory gating in normal subjects and to evaluate common extended sources during gating in the two modalities.

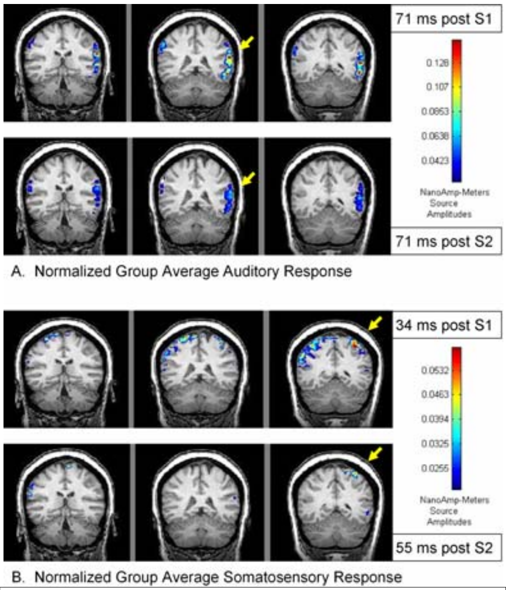

Figure 1. (A). Group average (n=10) MR-FOCUSS solution displaying amplitudes in NanoAmpMeters for the right hemisphere response to the left auditory stimulus showing S1 and S2 localizations. Arrows highlight auditory cortex. (B**)**. Group average (n=10) MR-FOCUSS solution amplitudes for the right hemisphere response to the left somatosensory stimulus showing S1 and S2 localizations. Arrows highlight somotosensory cortex

Methods

- Ten right handed normal controls (five females, 20-60 years, mean age 38.7 + 12.4) were recruited to study both auditory and somatosensory evoked fields.
- A 148-channel MEG system (4D Neuroimaging Magnes WH2500) recorded brain activity for Auditory and Somatosensory evoked fields (AEFs and SEFs)
- AEFs used S1-S2 paired-stimulus of tones separated by 500-ms interstimulus interval (ISI) with an intertrial interval (ITI) of 8 sec monaurally; 100 trials were collected per stimulus side.
- SEFs used S1-S2 somatosensory stimuli of finger taps (15-17 psi) to the middle finger with 500-ms ISI and 8 sec ITI, right & left sides separately for 100 trials.
- Epochs of 100 ms of pre-stimulus & 2 seconds of post-stimulus data. Digitized at 508 samples per second from 0.01 Hz - 100 Hz, filtered 3-50 Hz with 60 Hz notch, inspected for artifact then averaged.
- MR-FOCUSS, current density imaging technique, determined source amplitudes (Moran 2005) on a normal volumetric MRI scan (GE 1.5 T).
- Response to S1 and S2 used cortical activity within region of interest (ROI) 1.6 cm (~ 20 pixels) diameter on S1 response maximum. A source localization algorithm used a nearness threshold to establish ROI size so only S1 auditory cortical activity was included. ROIs contained 40–50 cortical model source locations.
- The S1 latency was determined post-stimulus by peak source amplitude between 40 and 80 ms for AEFs and between 30 and 130 ms for SEFs.
- The S2 latency was limited within 30 ms of the S1 latency.
- SEFs showed extended response with early peak response associated with initial sensory inputs from the finger and secondary late peak was observed ~45 ms for both the S1 and S2 inputs.
- Individual cortical responses were normalized to obtain an across subject average response shown in **Figure 1**.
- Gating ratio (S2/S1) were calculated as response to S2 peak source amplitude over response to S1 peak source amplitude, average results shown in **Figure 2**.
- Frontal locations, active at significance levels above 90%, were identified in S1 and S2 latency windows and designated superior, medial or inferior frontal.

Results

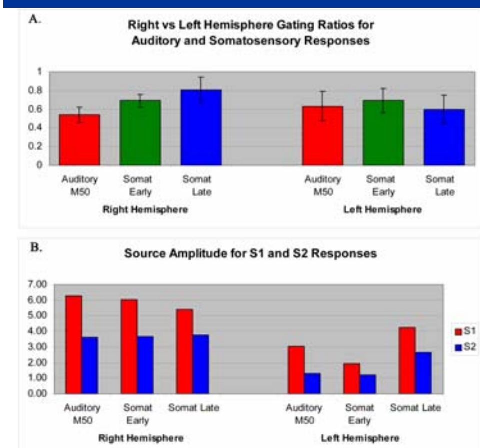

Figure 2. (A). Group average gating ratios (n = 10) for right and left hemisphere responses to auditory and somatosensory stimuli. Error bars indicate standard error for each calculated ratio. (B). Average source amplitude (n = 10) for S1 and S2 stimuli for auditory and somatosensory data.

AEF RESPONSES: S1 and S2 observed in all subjects at expected latencies

• RIGHT: S1: 6.3±4.8 nAm S2: 3.6±3.3 nAm S2/S1: 0.54±0.24
67±8 ms 69±10 ms

• LEFT: S1: 3.0±3.4 nAm S2: 1.3±1.4 nAm S2/S1: 0.63±0.52
66±10 ms 65±10 ms

• Active sources identified in the frontal lobe in 19/20 subjects for S1 response (both hemispheres) and in 15/20 subjects for the S2 response.

• S1 response shared at least one frontal region of activation with S2 response in the right hemisphere for 9/10 subjects. The left hemisphere response shared S1 and S2 frontal region activation in only 3/10 subjects.

SEF RESPONSES: S1 and S2 were observed in all subjects at expected latencies

• RIGHT: Early: S1: 6.1±3.7 nAm S2: 3.7±1.8 nAm S2/S1: 0.69±0.21
44±8 ms 41±7 ms

Late: S1: 5.4±3.3 nAm S2: 3.8±2.4 nAm S2/S1: 0.81±0.41
92±16 ms 82±14 ms

• LEFT: Early: S1: 1.8±1.5 nAm S2: 1.2±1.3 nAm S2/S1: 0.69±0.41
47±7 ms 44±6 ms

Late: S1: 3.9±6.3 nAm S2: 2.4±4.7 nAm S2/S1: 0.60±0.48
93±17 ms 94±17 ms

• Our early and late somatosensory latencies correspond to P50 and N80 responses elicited by electrical simulation.

• Active sources identified in the frontal lobe in 20/20 subjects for both S1 and S2 response in both hemispheres.

• S1 response shared at least one frontal region of activation with S2 response for 10/10 subjects for both right and left hemispheres.

Results

Frontal Activation in Auditory and Somatosensory Responses

• Activation of the same frontal areas for the S1 response in both the auditory and somatosensory tests for 10/10 subjects in the right hemisphere and 7/10 for the left hemisphere.

• For both the auditory and somatosensory tests, the S2 response had similar frontal active areas in 8/10 subjects in the right and 5/10 in the left hemispheres.

• **Figure 3** displays the extended cortical sources active in a typical subject.

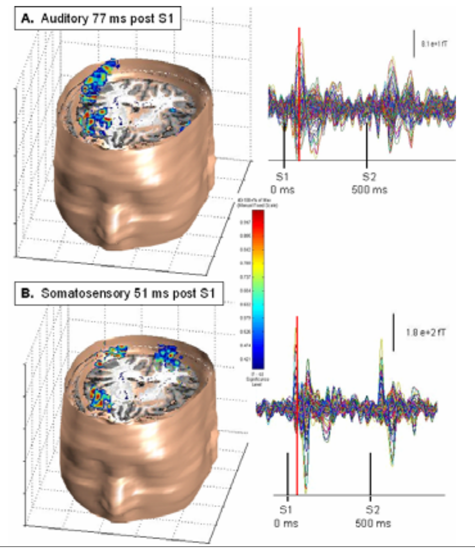

Figure 3. (A). Auditory response following S1 for one subject showing extended cortical sources. Also displayed are MEG waveforms with red line indicating latency of 77 ms. (B). Somatosensory response following S1 for same subject showing similar frontal sources. MEG waveforms are shown with red line indicating latency of 51 ms.

Conclusions

- Our current density technique, MR-FOCUSS, yielded gating ratios similar to previous literature values and localized extended frontal sources for the M50 generators beyond the sensory cortex following both the S1 and S2 stimuli.
- Frontal activation following either auditory or somatosensory stimulation is simultaneous to the activation in the expected sensory cortex. These areas of activation are consistent across modalities in 17/20 responses to S1 and 13/20 to S2 stimuli.
- First study to provide evidence of cross modal activation of the frontal cortex during gating and suggests that the frontal lobe has an important role in the neural mechanisms of habituation.
- This evidence for a crucial frontal lobe role in mediating sensory gating in multiple modalities for normal controls, provides groundwork to compare habituation deficits in patient populations (Weiland, 2008).

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